REMARKS

Claims 1 - 26 are still pending. Claims 2 and 9 – 26 are withdrawn from consideration. Claims 1 and 3 – 8 are currently under examination in this application.

Claims 1 and 3 – 8 were rejected under 35 USC 112, first paragraph for nonenablement. This rejection is respectfully traversed.

First, the examiner points to passages in the specification that mention the age-related decline in immune function as being a possible explanation for the increased incidence of neurodegenerative diseases with age. This does not mean, however, that age is the only determinative factor, and the specification does not state that it is. Rather, the specification as a whole is concerned with any decline in immune surveillance, whether from a disease state (see p. 6, line 19) or perhaps even nutritional. Also mentioned on page 6, lines 11 – 12, is that the effectiveness of the vaccine diminishes over time, so that booster vaccination is required. Such would occur at any age.

Thus, the statement in the Office Action that the invention is not enabled for neurodegenerative diseases that are *not* associated with aging should not be maintained, because it is based on the erroneous assumption that "age-related decline in immune function is the underlying physiological deficit that the instant invention is intended to treat." (See Office Action, page 4, lines 1 – 5.) The invention is intended to neutralize the effects of diphtheria toxin on EF-2; one

way to do this is to stimulate the immune system by (booster) vaccination with the toxoid. While the immune system may decline with age, it does not mean that the system doesn't work at all. For instance, many elderly people get flu vaccines every year that presumably work. If they didn't get the vaccinations, their immune system may not respond as well as younger people and they may get a worse case of the flu. That is, they may not fight off infections as well as younger people. The specification certainly does not state that older people are not responsive to vaccinations. Thus, the statement in the Office Action that "the specification itself provides guidance that the instant invention is not operative" is simply not correct.

Second, the Office Action states (p. 4, lines 11 -15) that there is no support in the McLay reference for Applicant's suggestion that decreased incidence of age-related cognitive decline in the military may be due to better attention to immunizations. The McLay reference was only cited for its interesting finding of decreased age-related cognitive decline in the military. It is true, as the Examiner states, that McLay had no satisfactory explanation for this fact. However, based on the present invention, it only makes sense that there is less cognitive decline due to neurodegeneration in a population that, by its tendency for regular immunizations, is better equipped immunity-wise to neutralize the ADP-ribosylating toxins. Applicant does not rely on the McLay reference for support in this instance; if McLay had suggested this, then it may have been suggestive of the present invention itself.

Third, on page 4 of the Office Action, the Examiner questions why there is not an increased incidence of diphtheria disease with age if Applicant's basis for the invention is correct. As stated in the paragraph bridging pages 6 and 7 and the first paragraph on page 7 of the specification, *C. diphtheria* and *P. aeroginosa* are known to exist in a chronic (low-level) carrier states. As such, the infection does not manifest acute disease, which is why it typically would be of no concern. The toxin released by such carrier-state infections is small enough to ordinarily be kept neutralized by a regularly functioning immune system. Thus, it is in those "carriers" whose immune system is waning, for whatever reason, that the toxin is not being adequately neutralized and is allowed to exert its effects on nerve cells.

Fourth, the Examiner's emphasis on age-related immune decline in the passage appearing at the top of page 5 of the Office Action causes him to question why AD occurs in "non-immune impaired younger individuals". However, there is no basis for the assumption that younger AD patients (e.g. late 40's or 50's) are "non-immune impaired". Moreover, as mentioned above, the present invention is not limited to the treatment of older individuals – it applies to any immune-compromised patients exhibiting neurological deficits.

Finally, the Office Action asserts the Johnson paper "teaches that hyperphosphorylation and not ADP-ribosylation had occurred to the EF-2 on the gels and it was hyperphosphorylation and not ADP-ribosylation that produced the

altered migrations..." It is noted that Applicant is an author on this paper, and the work was done in his laboratory. What the specification states is that, while hyperphosphorylation was observed, ADP-ribosylation was not ruled out by the techniques used in this work. Therefore, the work disclosed in this reference does not refute the present invention. In fact, subtle amounts of ADP-ribosylation may well have occurred, which in itself would lead to the hyperphosphorylation. This is what was meant by the passage in the specification referred to by the Examiner (which the undersigned prepared). That is, there was no conclusive evidence in the Johnson paper that ADP-ribosylation was not present, because the experiments did not rule it out.

Thus, Applicant submits that the specification provides sound scientific reasoning to support the enablement of the claimed invention. Carrier states of infection are known, for which the toxin is kept in check by an adequately functioning immune system. If the immune system declines, the toxin, which preferentially affects nerve cells, is allowed to exert its effects whereby the cells eventually die. A (booster) vaccination with the toxoid serves to boost the immune function toward the toxin, whereby cell death, and the associated clinical signs, is ameliorated. Nothing in the rejection adequately refutes this reasoning.

Accordingly, reconsideration and withdrawal of this rejection are deemed proper. The application has a presumption of patentability unless the patent office establishes a prima facie case of unpatentability, which has not been done in this instance.

Prompt allowance of this application is earnestly solicited. The Examiner is invited to contact the undersigned at the number or email listed below should he believe there are any remaining issues that could be more easily resolved by direct communication.

Respectfully submitted,

M. Elisa Lane
Registration No. 34,409
(filed under Rule 34)

On behalf of:
Panacea Pharmaceuticals, Inc.
207 Perry Parkway
Suite 2
Gaithersburg, Maryland 20877
Tel: (240) 243-8016
elisalane@panaceapharma.com